

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A molecular sensing apparatus comprising:

one or more electrode pairs, wherein at least one electrode pair in said one or more electrode pairs comprises:

a first electrode;

a second electrode; and

an insulator between said first electrode and said second electrode,

wherein ~~a portion of said insulator~~ comprises a channel ~~is removed~~ between said first electrode and said second electrode ~~thereby forming a channel within said insulator;~~
and

wherein said first electrode and said second electrode are separated by less than 30 nanometers ~~a distance that would allow a biological macromolecule or biological macromolecule/analyte complex to connect said first electrode to said second electrode and said apparatus is configured to permit the formation of a plurality of independent, electrically coupled binding agent/analyte complexes between said first electrode and said second electrode.~~

2-4. (Canceled)

5. (Previously presented) The molecular sensing apparatus of claim 1, wherein said insulator has a resistivity greater than 10^{-3} ohm-meters.

6. (Previously presented) The molecular sensing apparatus of claim 1, wherein said insulator is selected from the group consisting of SiO₂, TiO₂, ZrO₂, quartz, porcelain, ceramic, polystyrene, TEFLON, and an insulating oxide or sulfide of a transition metal in the periodic table of the elements.

7. (Previously presented) The molecular sensing apparatus of claim 1, wherein said first electrode and said second electrode are separated by a distance in the range of 1 Angstrom to 10¹⁰ Angstroms.

8. (Canceled)

9. (Previously presented) The molecular sensing apparatus of claim 1, wherein at least one of said first electrode and said second electrode has a resistivity of less than 10⁻² ohm-meters.

10. (Previously presented) The molecular sensing apparatus of claim 1, wherein at least one of said first electrode and said second electrode has a resistivity of less than 10⁻³ ohm-meters.

11. (Previously presented) The molecular sensing apparatus of claim 1, wherein said first electrode and said second electrode each comprises a material selected from the group consisting of ruthenium, osmium, cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and carbon nanotube.

12. (Previously presented) The molecular sensing apparatus of claim 1, wherein at least one of said first electrode and said second electrode is functionalized with a chemical group that can be derivatized or crosslinked.

13. (Previously presented) The molecular sensing apparatus of claim 12, wherein said chemical group is selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

14. (Previously presented) The molecular sensing apparatus of claim 1, wherein at least one of said first electrode and said second electrode bears a self-assembled monolayer (SAM).

15. (Previously presented) The molecular sensing apparatus of claim 14, wherein said SAM comprises a compound selected from the group consisting of an alkanethiol, a phospholipid, a bola amphiphile, and an oligo (phenylenevinylene).

16-19. (Canceled)

20. (Previously presented) The molecular sensing apparatus of claim 1, further comprising a substrate that supports the first electrode and the second electrode, wherein the first electrode and the second electrode are integrated with the substrate.

21. (Previously presented) The molecular sensing apparatus of claim 1, wherein the first electrode and the second electrode are integrated with the insulator to form a substrate.

22. (Previously presented) The molecular sensing apparatus of claim 1, wherein said first electrode comprises a surface with a shape selected from the group consisting of convex, concave, textured, corrugated, patterned uniformly, and randomly patterned.

23. (Previously presented) The molecular sensing apparatus of claim 1, wherein said first electrode and said second electrode are oriented in a formation selected from the group consisting of annular, planar, and orthogonal.

24. (Previously presented) The molecular sensing apparatus of claim 1, wherein the first electrode has a first surface and a said second electrode has a second surface, wherein the first surface is not coplanar to the second surface.

25. (Currently amended) The apparatus of claim 1, wherein said as at least one electrode pair comprises a first electrode pair and a second electrode pair.

26 (Previously presented) The molecular sensing apparatus of claim 1, wherein said one or more electrode pairs are at least 10 electrode pairs.

27. (Previously presented) The molecular sensing apparatus of claim 1, wherein said one or more electrode pairs are at least 1,000 electrode pairs.

28. (Previously presented) The molecular sensing apparatus of claim 1, wherein said one or more electrode pairs comprises about 10^2 to 10^{10} electrode pairs.

29. (Previously presented) The molecular sensing apparatus of claim 1, the molecular sensing apparatus further comprising a measurement device electrically coupled to

each first electrode and to each second electrode of each electrode pair in said at least one electrode pair.

30. (Previously presented) The molecular sensing apparatus of claim 29, wherein said measurement device measures an electromagnetic property selected from the group consisting of direct electric current, alternating electric current, permittivity, resistivity, electron transfer, electron tunneling, electron hopping, electron transport, electron conductance, voltage, electrical impedance, signal loss, dissipation factor, resistance, capacitance, inductance, magnetic field, electrical potential, charge and magnetic potential.

31. (Previously presented) The molecular sensing apparatus of claim 1, further comprising an electrical circuit electrically coupled to the first electrode and the second electrode.

32. (Previously presented) The molecular sensing apparatus of claim 31, wherein said electrical circuit comprises an electric signal gating system.

33. (Previously presented) The molecular sensing apparatus of claim 32, wherein said electric signal gating system comprises a CMOS gating system.

34. (Previously presented) The apparatus of claim 25, wherein
a first biological macromolecule is attached to the first electrode and the second electrode in the first electrode pair, and

a second biological macromolecule is attached to the first electrode and the second electrode in the second electrode pair; wherein the first biological molecule and the second biological molecule are the same.

35. (Previously presented) The apparatus of claim 25, wherein

a first biological macromolecule is attached to the first electrode and the second electrode in the first electrode pair, and

a second biological macromolecule is attached to the first electrode and the second electrode in the second electrode pair; wherein the first biological molecule and the second biological molecule are different.

36. (Previously presented) The molecular sensing apparatus of claim 1, further comprising a computer electrically coupled to the first electrode and the second electrode.

37. (Previously presented) The molecular sensing apparatus of claim 1, wherein at least one of the first electrode and the second electrode comprises a semiconductor material.

38. (Previously presented) The molecular sensing apparatus of claim 37, wherein said semiconductor material has a resistivity ranging from $10^{-6} \Omega\text{-m}$ to $10^7 \Omega\text{-m}$.

39. (Previously presented) The molecular sensing apparatus of claim 37, wherein the semiconductor material is selected from the group consisting of silicon, dense silicon carbide, boron carbide, Fe_3O_4 , germanium, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum

arsenide, mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSc. CdS, ZnTc, GaSc, CdSe, CdTe, GaAs, InP, GaSb, EnAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide.

40. (Canceled)

41. (Withdrawn) A method of making a molecular sensing apparatus, said method comprising.

providing a first electrode and a second electrode separated by an insulator;

contacting said first and said second electrode with a first solution comprising a biological macromolecule;

placing a charge on said first electrode to attract said biological macromolecule to said first electrode where said macromolecule attaches to said first electrode to form an attached macromolecule; and

placing a charge on said second electrode to attract a portion of said attached macromolecule to said second electrode where said macromolecule attaches to said second electrode.

42. (Withdrawn) The method of 41, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a proteins, a polysaccharide, a lectin, and a lipid.

43. (Withdrawn) The method of claim 41, wherein said biological macromolecule is functionalized with a chemical group selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an

alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

44. (Withdrawn) The method of claim 41, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin and a lipid.

45. (Withdrawn) The method of claim 41, wherein said biological macromolecule is a nucleic acid.

46. (Withdrawn) The method of claim 41, wherein said insulator has a resistivity of greater than about $10^{-3} \Omega\text{-m}$.

47. (Withdrawn) The method of claim 41, wherein said insulator is selected from the group containing SiO_2 , TiO_2 , ZrO_2 , porcelain, ceramic, quartz, high resistivity plastic, and an insulating oxide or sulfide of the transition metals in the periodic table of the elements.

48. (Withdrawn) The method of 41, wherein said first electrode and said second electrode are separated by a distance range from about 1 to about 10^{10} Angstroms.

49. (Withdrawn) The method of claim 41, wherein said first electrode and said second electrode are separated by a distance less than about 70 Angstroms.

50. (Withdrawn) The method of claim 41, wherein said first electrode and said second electrode have a resistivity of less than about $10^{-3} \Omega\text{-m}$.

51. (Withdrawn) The method of claim 41, wherein said first electrode and said second electrode comprise a material selected from the group consisting of ruthenium, osmium,

cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and a carbon nanotube.

52. (Withdrawn) The method of claim 41, wherein said first electrode is functionalized to bear a chemical group capable of being further derivatized or crosslinked.

53. (Withdrawn) The method of claim 52, wherein the said chemical group is selected from the group consisting of functionalized with a chemical group selected from a sulfate, a sulfhydryl an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkene, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, a group activatable by an electric potential.

54. (Withdrawn) The method of claim 41, wherein said biological macromolecule is attached to said first electrode by an electrically conductive linker.

55. (Withdrawn) The method of claim 54, wherein said linker is selected from the group consisting of DFDNB, DST, ABH, ANB-NOS, EDC, NHS-ASA, and SIA.

56. (Withdrawn) The method of claim 54, wherein said linker is oligo(phenylenevinylene).

57. (Withdrawn) The method of claim 41, further comprising a substrate to support the first electrode and the second electrode, wherein the first electrode and the second electrode are integrated with the substrate.

58. (Withdrawn) The method of claim 41, further comprising a substrate with the first electrode and the second electrode, wherein the first electrode and the second electrode are integrated with the insulator to form a substrate.

59. (Withdrawn) The method of claim 41, wherein the first electrode and the second electrode provide a first electrode pair, the molecular sensing apparatus further comprising a second electrode pair comprising a second first electrode and a second second electrode.

60. (Withdrawn) The method of claim 59, wherein said apparatus comprises at least 3 electrode pairs.

61. (Withdrawn) The method of claim 59, wherein said apparatus comprises at least 100 electrode pairs.

62. (Withdrawn) The method of claim 59, wherein said apparatus comprises about 10^2 to about 10^{10} electrode pairs.

63. (Withdrawn) The method of claim 59, further comprising:

contacting said second electrode pair with a second solution comprising a second biological macromolecule;

placing a charge on a first electrode of said second electrode pair to attract said second biological macromolecule to said first electrode of said second electrode pair whereby said second biological macromolecule attaches to said first electrode to form an attached second macromolecule; and

placing a charge on said second electrode of said second electrode pair to attract a portion of said attached second macromolecule to said second electrode whereby said second macromolecule attaches to said second electrode of said second electrode pair.

64. (Withdrawn) The method of claim 63, wherein said apparatus comprises a third electrode pair.

65. (Withdrawn) The method of claim 63, wherein said apparatus comprises greater than 3 electrode pairs.

66. (Withdrawn) The method of claim 63, wherein said first solution and said second solution are the same.

67. (Withdrawn) The method of claim 63, wherein said first solution and said second solution are different.

68. (Withdrawn) The method of claim 63, wherein said first biological molecule and said second biological molecule are the same.

69. (Withdrawn) The method of claim 63, wherein said first biological molecule and said second biological molecule are the different.

70. (Withdrawn) The method of claim 41, wherein at least one of said first electrode and said second electrode comprise a semi-conducting material.

71. (Withdrawn) The method of claim 70, wherein the semi-conductor material has a resistivity in the range of $10^{-6} \Omega\text{-m}$ to $10^{-7} \Omega\text{-m}$.

72. (Withdrawn) The method of claim 70, wherein the semi-conducting material is selected from the group consisting of silicon, dense silicon carbide, boron carbide, Fe_3O_4 , germanium, silicone germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide.

73. (Withdrawn) A method of detecting an analyte said method comprising:

i) providing molecular sensing apparatus comprising a first electrode and a second electrode separated by an insulator where said first electrode has a biological macromolecule attached thereto;

ii) contacting the attached macromolecule with said analyte whereby said analyte binds to said macromolecule thereby forming a macromolecule/analyte complex;

iii) placing a charge on said second electrode attract a portion of said bound analyte to said second electrode where said analyte is bound to said second electrode such that said macromolecule/analyte complex forms a connection between said first electrode and said second electrode; and

iv) detecting the connection between said first and said second electrode.

74. (Withdrawn) The method of claim 73, wherein said providing comprises:

contacting said first electrode with a first solution comprising said biological macromolecule; and

placing a charge on said first electrode whereby said charge attracts said biological macromolecule to said electrode and said biological macromolecule attaches to said electrode.

75. (Withdrawn) The method of claim 73, wherein said placing a charge, further comprising placing a charge on said first electrode opposite to the charge on said second electrode.

76. (Withdrawn) The method of claim 73, wherein said detecting comprises detecting an electromagnetic property selected from the group consisting of direct electric current, alternating electric current, permittivity, resistivity, electron transfer, electron tunneling, electron hopping, electron transport, electron conductance, voltage, electrical impedance, signal loss, dissipation factor, resistance, capacitance, inductance, magnetic field, electrical potential, charge, and magnetic potential.

77. (Withdrawn) The method of claim 73, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin, and a lipid.

78. (Withdrawn) The method of claim 78, wherein, said biological macromolecule is a nucleic acid.

79. (Withdrawn) The method of claim 78, wherein said biological macromolecule is functionalized with a chemical group selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

80. (Withdrawn) The method of claim 73, wherein said insulator has a resistivity greater than $10^{-3} \Omega\text{-m}$.

81. (Withdrawn) The method of claim 73, wherein said insulator is selected from the group consisting of SiO_2 , TiO_2 , ZrO_2 , porcelain, ceramic, a high resistivity plastic, and an insulating oxide or sulfide of a transition metal in the periodic table of the elements.

82. (Withdrawn) The method of claim 73, wherein said first electrode and said second electrode are separated by a distance less than about 70 Angstroms.

83. (Withdrawn) The method of claim 73, wherein said first electrode and said second electrode are separated by a distance ranging from about 1 to about 10^{10} Angstroms

84. (Withdrawn) The method of claim 73, wherein said first electrode and said second electrode have a resistivity of less than about $10^{-2} \Omega\text{-m}$.

85. (Withdrawn) The method of claim 73, wherein said first electrode comprises a semiconductor material.

86. (Withdrawn) The method of claim 88, wherein said semi-conductor material has a resistivity ranging from about $10^{-6} \Omega\text{-m}$ to about $10^{-7} \Omega\text{-m}$.

87. (Withdrawn) The method of claim 88, wherein the semi-conducting material is selected from the group consisting of silicon, dense silicon carbide, boron carbide, Fe_3O_4 , germanium, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide,

mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe.

CdTe, GaAs, hip, GaSb, InAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide.

88. (Withdrawn) The method of claim 73, wherein said first electrode and said second electrode are formed from a material selected from the group consisting of ruthenium, osmium, cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and a carbon nanotube.

89. (Withdrawn) The method of 73, wherein at 1 said first electrode is functionalized to bear a chemical group capable of being further derivatized or crosslinked.

90. (Withdrawn) The method of claim 89, wherein the said chemical group is selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

91. (Withdrawn) The method of claim 89, wherein said functionalized biological macromolecule is attached to said first electrode by an electrically conductive linker.

92. (Withdrawn) The method of claim 91, wherein said linker is selected from the group consisting DFDNB, DST, ABM, ANB-NOS, EDC, NHS-ASA, and SIA.

93. (Withdrawn) The method of claim 91, wherein said linker is oligo(phenylenevinylene).

94. (Withdrawn) The method of claim 73, wherein the first electrode and the second electrode are integrated with a substrate.

95. (Withdrawn) The method of claim 73, wherein the first electrode and the second electrode are integrated with the insulator to form a substrate.

96. (Withdrawn) The method of claim 73, wherein the first electrode and the second electrode provide a first electrode pair, the molecular sensing apparatus further comprising a second electrode.

97. (Withdrawn) The method of claim 96, wherein said apparatus comprises at least 3 electrode pairs.

98. (Withdrawn) The method of claim 96, wherein said apparatus comprises at least 100 electrode pairs.

99. (Withdrawn) The method of claim 96, wherein said apparatus comprises from about 10^2 to about 10^{10} electrode pairs.

100. (Withdrawn) The method of claim 96 further comprising performing steps ii, iii, and iv with said second electrode pair.

d) contacting the second biological macromolecule with said sample potentially comprising said analyte so that any analyte in said sample binds to said second biological macromolecule thereby forming a second biological macromolecule/analyte complex;

e) placing a charge on said fourth electrode to attract a portion of any said second biological macromolecule/analyte complex to said fourth electrode thereby forming a connection between said third electrode and said fourth electrode; and

f) detecting any said connection between the third electrode and the fourth electrode.

101. (Withdrawn) The method of claim 96, wherein the biological macromolecule on said first electrode pair is different than the biological macromolecule attached to the second electrode pair.

102. (Withdrawn) A method of detecting an analyte, said method comprising:

i) providing a molecular sensing apparatus comprising a first electrode and a second electrode separated by a spacer where said first electrode has a first biological macromolecule attached thereto and said second electrode has a second biological macromolecule attached thereto;

ii) contacting the first attached macromolecule and the a second attached macromolecule with said analyte whereby said analyte binds to the first macromolecule and to the second macromolecule thereby forming a macromolecule/analyte complex forming a connection between said first electrode and said second electrode; and

iii) detecting the connection between said first and said second electrode.

103. (Withdrawn) The method of 102, wherein said providing comprises:

contacting said first electrode with a first solution comprising said first biological macromolecule; and

placing a charge on said first electrode whereby said charge attracts said first biological macromolecule to said electrode and said biological macromolecule attaches to said electrode.

104. (Withdrawn) The method of claim 102, wherein said detecting comprises detecting an electromagnetic property selected from the group consisting of direct electric current, alternating electric current, permittivity, resistivity, electron transfer, electron tunneling, electron hopping, electron transport, electron conductance, voltage, electrical impedance, signal loss, dissipation factor, resistance, capacitance, inductance, magnetic field, electrical potential, charge and magnetic potential.

105. (Withdrawn) The method of claim 102, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin, and a lipid.

106. (Withdrawn) The method of claim 102, wherein said biological macromolecule is a nucleic acid.

107. (Withdrawn) The method of claim 106, wherein said biological macromolecule is functionalized with a chemical group selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

108. (Withdrawn) The method of claim 102, wherein said insulator has a resistivity greater than $10^{-3} \Omega\text{-m}$.

109. (Withdrawn) The method of claim 102, wherein said insulator is selected from the group consisting of SiO_2 , TiO_2 , ZrO_2 , ceramic, porcelain, a high resistivity plastic, and an insulating oxide or sulfide of a transition metal in the periodic table of the elements.

110. (Withdrawn) The method of claim 102, wherein said first electrode and said second electrode are separated by a distance less than about 70 Angstroms.

111. (Withdrawn) The method of claim 102, wherein said first electrode and said second electrode are separated by a distance ranging from about 1 to about 10^{10} Angstroms.

112. (Withdrawn) The method of claim 102, wherein said first electrode and said second electrode have a resistivity of less than about $10^{-2} \Omega\text{-m}$.

113. (Withdrawn) The method of claim 102, wherein said first electrode and said second electrode comprise a material selected from the group consisting of ruthenium, osmium, cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, indium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and a carbon nanotube.

114. (Withdrawn) The method of claim 102, wherein at least one of the first electrode and the second electrode comprises a semi-conductor material.

115. (Withdrawn) The method of claim 114, wherein said semi-conductor material has a resistivity ranging from about $10^{-3} \Omega\text{-cm}$ to about $10^{-7} \Omega\text{-cm}$.

116. (Withdrawn) The method of claim 114, wherein said semi-conducting material is selected from the group consisting of silicon, dense silicon carbide, boron carbide, Fe_3O_4 , germanium, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide.

117. (Withdrawn) The method of claim 102, wherein said first electrode and said second electrode are formed from a material selected from the group consisting of ruthenium, osmium, cobalt, rhodium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and a carbon nanotube.

118. (Withdrawn) The method of claim 102, wherein at least one of the said first electrode and second electrode is functionalized to contain a chemical group capable of being further derivatized or crosslinked.

119. (Withdrawn) The method of claim 118, wherein the said chemical group is selected from the group consisting of an a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light activatable group, and a group activatable by an electric potential.

120. (Withdrawn) The method of claim 118, wherein said functionalized biological macromolecule is attached to said first electrode by an electrically conductive linker.

121. (Withdrawn) The method of claim 120, wherein said linker is selected from the group consisting DFDNB, DST, ABH, ANB-NOS, EDC, NHS-ASA, and SIA.

122. (Withdrawn) The method of claim 120, wherein said linker is oligo(phenylenevinylene).
123. (Withdrawn) The method of claim 102, wherein the first electrode and the second electrode are integrated with a substrate.
124. (Withdrawn) The method of claim 102, wherein the first electrode and the second electrode are integrated with the insulator to form a substrate.
125. (Withdrawn) The method of claim 102, wherein the first electrode and the second electrode provide a first electrode pair, the molecular sensing apparatus further comprising a second electrode pair comprising a second first electrode and a second electrode.
126. (Withdrawn) The method of claim 125, wherein said apparatus comprises at least 3 electrode pairs.
127. (Withdrawn) The method of claim 125, wherein said apparatus comprises at least 100 electrode pairs.
128. (Withdrawn) The method of claim 132, wherein said apparatus comprises from about 10^2 to about 10^{10} electrode pairs.
129. (Withdrawn) The method of claim 125, further comprising performing steps ii and iii with said second electrode pair
- c) contacting the analyte with the third biological macromolecule and the fourth biological macromolecule thereby forming a second macromolecule/analyte complex comprising the third biological macromolecule, the fourth biological macromolecule and the analyte,

wherein the macromolecule/analyte complex connects said first electrode and said second electrode in said second electrode pair; and

d) detecting the connection between said first electrode and said second electrode in said second electrode pair.

130. (Withdrawn) The method of claim 125, wherein at least one of the biological macromolecule on an electrode of the second pair is different from either of the biological macromolecules on the electrodes of the first electrode pair.

131. (Withdrawn) The method of claim 125, wherein the biological on the electrode of the second electrode pair are different from the biological macromolecules on the electrodes of the first electrode pair.

132. (Withdrawn) A method of detecting an analyte, said method comprising:

i) providing a molecular sensing apparatus comprising a first electrode and a second electrode separated by a spacer where a biological macromolecule forms a connection between said first electrode and said second electrode;

ii) detecting the connection between said first and said second electrode;

iii) contacting the attached macromolecule with said analyte whereby said analyte binds to said macromolecule forming a macromolecule/analyte complex; and

iv) detecting the difference in the connection between said first electrode and said second electrode.

133. (Withdrawn) The method of claim 132, wherein said contacting comprises placing a charge on said first electrode whereby said charge attracts said analyte to said biological macromolecule.

134. (Withdrawn) The method of claim 132, wherein said providing comprises contacting said first electrode with a first solution comprising said biological macromolecule; and

placing a charge on said first electrode whereby said charge attracts said biological macromolecule to said electrode and said biological macromolecule attaches to said electrode and

placing a charge on said second electrode to attract a portion of said bound macromolecule to said second electrode where said macromolecule is bound to said second electrode such that said macromolecule forms a connection between said first electrode and said second electrode.

135. (Withdrawn) The method of claim 132, wherein said placing a charge comprises placing a charge on said first electrode opposite to the charge on said second electrode.

136. (Withdrawn) The method of claim 132, wherein said detecting comprises detecting an electromagnetic property selected from the group consisting of direct electric current, alternating electric current, permittivity, resistivity, electron transfer, electron tunneling, electron hopping, electron transport, electron conductance, voltage, electrical impedance, signal loss, dissipation factor, resistance, capacitance, inductance, magnetic field, electrical potential, charge and magnetic potential.

137. (Withdrawn) The method of claim 132, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin or a lipid.

138. (Withdrawn) The method of claim 132, wherein said biological macromolecule is a nucleic acid.

139. (Withdrawn) The method of claim 132, wherein said analyze is a protein or protein complex.

140. (Withdrawn) The method of claim 132, wherein said biological macromolecule is functionalized with a chemical group consisting of a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl, bromine, iodine, chlorine, a chemical group that can be activated by light, and a chemical group that can be activated by the application of an electrical potential.

141. (Withdrawn) The method of claim 132, wherein said insulator is selected from the group consisting of elements, compounds or substances that have resistivities greater than $10^{-3} \Omega\text{-m}$.

142. (Withdrawn) The method of claim 141, wherein said insulator is selected from the group containing SiO_2 , TiO_2 , ZrO_2 , porcelain, polystyrene, polystyrene, organic compounds produced by polymerization having a resistivity greater than $10^{-3} \Omega\text{-m}$, and insulating oxides or sulfides of the transition metals in the periodic table of the elements.

143. (Withdrawn) The method of claim 132, wherein said first electrode and said second electrode are separated by a distance less than about 70 Angstroms.

144. (Withdrawn) The method of claim 132, wherein said first electrode and said second electrode are separated by a distance in the range of 1 to 10^9 Angstroms.

145. (Withdrawn) The method of claim 132, wherein at least one said first electrode and said second electrode are formed of a material selected from the group consisting of elements, compounds or substances that have resistivities of less than $10^{-2} \Omega\text{-m}$.

146. (Withdrawn) The method of claim 145, wherein the said first electrode and said second electrode are formed from a material selected from the group consisting of, ruthenium, osmium, cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon or carbon nanotubes or alloys or compounds of these materials.

147. (Withdrawn) The method of claim 132, wherein at least one of the first electrode and the second electrode comprises a semiconductor material.

148. (Withdrawn) The method of claim 132, wherein said semi-conductor material has a resistivity ranging from about $10^{-2} \Omega\text{-m}$ to about $10^9 \Omega\text{-m}$.

149. (Withdrawn) The method of claim 148, wherein the semi-conducting material is selected from the group consisting of silicon, dense silicon carbide, boron carbide,

Fe₃O₄, germanium, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, tungsten disulfide, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, PbS, InSb, PbTe, and PbSe.

150. (Withdrawn) The method of claim 132, wherein at least one of said first electrode and second electrode is functionalized to contain a chemical group capable of being further derivatized or crosslinked.

151. (Withdrawn) The method of claim 132, wherein said chemical group is selected from the group consisting of a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, an alkene, an alkyne, a hydroxyl group, bromine, iodine, chlorine, a chemical group that can be activated by light of wavelength ranging from 190 nm to 700 nm, a fluorinated aryl azide, a benzophenone, (R,S)-1-(3,4 (methylene-dioxy)-6-nitrophenyl) ethyl chloroformate [-] (MeNPOC), N-((2-pyridyl, ethyl)-4-azido) salicylamide or a chemical group that can be activated by the application of an electrical potential, such as S-benzyloxycarbonyl derivatives, S-benzyl thioethers, S-phenyl thioethers, S-4-picolyl thioethers, S-2,2,2-trichloroethoxycarbonyl derivatives, S-triphenylmethyl thioethers.

152. (Withdrawn) The method of claim 132, wherein said biological macromolecule is attached to said first electrode by an electrically conductive linker.

153. (Withdrawn) The method of claim 132, wherein said linker is selected from the group consisting of chemical crosslinkers capable of linking functional groups, such as DFDNB, DST, ABH, ANB-NOS, EDC, NHS, NHS-ASA, SIA.

154. (Withdrawn) The method of claim 132, wherein said linker is an oligo(phenylenevinylene).
155. (Withdrawn) The method of claim 132, wherein said apparatus further comprises substrate to support the first electrode and the second electrode, wherein the first electrode and the second electrode are integrated with the substrate.
156. (Withdrawn) The method of claim 132, wherein said apparatus further comprises a substrate in which the first electrode and the second electrode are integrated with the insulator to form the substrate.
157. (Withdrawn) The method of claim 132, wherein the first electrode and the second electrode provide a first electrode pair, the molecular sensing apparatus further comprising a second electrode pair comprising a second first electrode and a second second electrode.
158. (Withdrawn) The method of claim 157, wherein said apparatus comprises at least 3 electrode pairs.
159. (Withdrawn) The method of claim 157, wherein said apparatus comprises at least 100 electrode pairs.
160. (Withdrawn) The method of claim 157, wherein said apparatus comprises from about in the range of 10^2 to 10^{10} electrode pairs.
161. (Withdrawn) The method of claim 157, further comprising; performing steps ii, iii and iv with the second electrode pair

- d) detecting an electrical connection between the first electrode and the second electrode in the second electrode pair;
- e) contacting the second biological macromolecule that is connected to said first electrode and said second electrode in said second electrode pair with a second analyte whereby said second analyte binds to said second biological macromolecule thereby forming a second macromolecule/analyte complex comprising said second biological macromolecule and said second analyte; and
- f) detecting a difference in the electrical connections between said first electrode and said second electrode in said second electrode pair.

162. (Withdrawn) The method of claim 157, wherein the biological macromolecule attached to said first electrode pair is the same as the biological macromolecule attached to said second electrode pair.

163. (Withdrawn) The method of claim 157, wherein the biological macromolecule attached to said first electrode pair is different from the biological macromolecule attached to said second electrode pair.

164. (Withdrawn) The method of claim 157, wherein the analyte attached to said first electrode pair is the same as the analyte attached to said second electrode pair.

165. (Withdrawn) The method of claim 157, wherein the analyte attached to said first electrode pair is different from the analyte attached to said second electrode pair.

166. (Currently amended) A molecular sensing apparatus comprising one or more electrode pairs in [[a]] an insulating substrate, wherein a first electrode pair in said one or more electrode pairs comprises a first electrode and a second electrode, wherein said first electrode and said second electrode are separated by less than 30 nanometers and said apparatus is configured to permit the formation of a plurality of independent, electrically coupled binding agent/analyte complexes between said first electrode and said second electrode; ~~a portion of the substrate is removed between said first electrode and said second electrode thereby forming~~ and a channel within said insulating substrate, said channel having with walls formed by said first electrode and said second electrode in said first electrode pair.

167. (Canceled)

168. (Previously presented) The molecular sensing apparatus of claim 166 wherein a biological macromolecule connects said first electrode and said second electrode.

169. (Previously presented) The molecular sensing apparatus of claim 168 wherein said biological macromolecule is a nucleic acid.

170. (Previously presented) The molecular sensing apparatus of claim 169 wherein said nucleic acid is a deoxyribonucleic acid or a ribonucleic acid.

171 – 172 (Canceled)

173. (Previously presented) The molecular sensing apparatus of claim 166 wherein at least one of said first electrode and said second electrode has a resistivity of less than 10^{-3} ohm-meters.

166. (Currently amended) A molecular sensing apparatus comprising one or more electrode pairs in [[a]] an insulating substrate, wherein a first electrode pair in said one or more electrode pairs comprises a first electrode and a second electrode, wherein said first electrode and said second electrode are separated by less than 30 nanometers and said apparatus is configured to permit the formation of a plurality of independent, electrically coupled binding agent/analyte complexes between said first electrode and said second electrode;~~a portion of the substrate is removed between said first electrode and said second electrode thereby forming~~ and a channel within said insulating substrate, said channel having with walls formed by said first electrode and said second electrode in said first electrode pair.

167. (Canceled)

168. (Previously presented) The molecular sensing apparatus of claim 166 wherein a biological macromolecule connects said first electrode and said second electrode.

169. (Previously presented) The molecular sensing apparatus of claim 168 wherein said biological macromolecule is a nucleic acid.

170. (Previously presented) The molecular sensing apparatus of claim 169 wherein said nucleic acid is a deoxyribonucleic acid or a ribonucleic acid.

171 – 172. (Canceled)

173. (Previously presented) The molecular sensing apparatus of claim 166 wherein at least one of said first electrode and said second electrode has a resistivity of less than 10^{-3} ohm-meters.

174. (Previously presented) The molecular sensing apparatus of claim 166

wherein said first electrode and said second electrode comprise a material selected from the group consisting of ruthenium, osmium, cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and carbon nanotube.

175. (Previously presented) The molecular sensing apparatus of claim 166

wherein at least one of said first electrode and said second electrode is functionalized with a chemical group that can be derivatized or crosslinked.

176. (Previously presented) The molecular sensing apparatus of claim 175

wherein said chemical group is a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl, a bromine, an iodine, a chlorine, a light-activatable group, or a group activatable by an electric potential.

177. (Previously presented) The molecular sensing apparatus of claim 166

wherein at least one of said first electrode and said second electrode is coated with a self-assembled monolayer.

178. (Previously presented) The molecular sensing apparatus of claim 177

wherein said self-assembled monolayer comprises a compound selected from the group consisting of an alkanethiol, a phospholipid, a bola amphiphile, and an oligo(phenylenevinylene).

179. (Previously presented) The molecular sensing apparatus of claim 168

wherein the biological macromolecule is attached to the first electrode by a thiol group.

180. (Previously presented) The molecular sensing apparatus of claim 168

wherein the biological macromolecule is attached to the first electrode by a phosphonate.

181. (Previously presented) The molecular sensing apparatus of claim 168

wherein the biological macromolecule is attached to said first electrode by a linker.

182. (Previously presented) The molecular sensing apparatus of claim 181

wherein said linker is selected from the group consisting of DFDNB, DST, ABH, ANB-NOS, EDC, NHS-ASA, and SIA.

183. (Previously presented) The molecular sensing apparatus of claim 166

wherein the first electrode has a first surface and the second electrode has a second surface, and wherein the first surface is not coplanar to the second surface.

184. (Previously presented) The molecular sensing apparatus of claim 166

wherein said one or more electrode pairs comprise at least three electrode pairs.

185. (Previously presented) The molecular sensing apparatus of claim 166

wherein said one or more electrode pairs comprise at least 10,000 electrode pairs.

186. (Previously presented) The molecular sensing apparatus of claim 166

wherein said one or more electrode pairs comprises 10^2 to 10^{10} electrode pairs.

187. (Previously presented) The molecular sensing apparatus of claim 166 the

apparatus further comprising a measurement device electrically coupled to the first electrode and to the second electrode said first electrode pair.

188. (Previously presented) The molecular sensing apparatus of claim 187

wherein said measurement device measures an electromagnetic property selected from the group consisting of direct electric current, alternating electric current, permittivity, resistivity, electron transfer, electron tunneling, electron hopping, electron transport, electron conductance, voltage, electrical impedance, signal loss, dissipation factor, resistance, capacitance, inductance, magnetic field, electrical potential, charge and magnetic potential.

189. (Previously presented) The molecular sensing apparatus of claim 166 further comprising an electrical circuit electrically coupled to the first electrode and the second electrode of said first electrode pair.

190. (Previously presented) The molecular sensing apparatus of claim 189 wherein said electrical circuit comprises an electric signal gating system.

191. (Previously presented) The molecular sensing apparatus of claim 166 wherein said biological molecule connects to said first electrode and said second electrode in said first electrode pair.

192. (Previously presented) The molecular sensing apparatus of claim 166 wherein

a first biological macromolecule is attached to said first electrode in said first electrode pair, and

a second biological macromolecule is attached to said second electrode in said first electrode pair.

193. (Previously presented) The molecular sensing apparatus of claim 166 further comprising a computer electrically coupled to the first electrode and the second electrode of at least one electrode pair in said one or more electrode pairs.

194. (Previously presented) The molecular sensing apparatus of claim 166 wherein at least one of the first electrode and the second electrode in an electrode pair in said one or more electrode pairs comprises a semiconductor material.

195. (Previously presented) The molecular sensing apparatus of claim 194 wherein said semiconductor material has a resistivity between $10^{-6} \Omega\text{-m}$ and $10^{-7} \Omega\text{-m}$.

196. (Previously presented) The molecular sensing apparatus of claim 194 wherein the semiconductor material is selected from the group, consisting of silicon, dense silicon carbide, boron carbide, Fe_3O_4 , germanium, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide.

197. (Previously presented) The molecular sensing apparatus of claim 1, wherein a biological macromolecule or macromolecule/analyte complex connects said first electrode and said second electrode in said first electrode pair.

198. (Previously presented) The molecular sensing apparatus of claim 197 wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin, and a sugar.

199. (Previously presented) The molecular sensing apparatus of claim 197

wherein said biological macromolecule is a deoxyribonucleic acid or a nucleic acid.

200. (Previously presented) The molecular sensing apparatus of claim 197

wherein said biological macromolecule is functionalized with a chemical group selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

201. (Previously presented) The molecular sensing apparatus of claim 197

wherein the biological macromolecule is attached to the first electrode by a thiol group.

202. (Previously presented) The molecular sensing apparatus of claim 197

wherein the biological macromolecule is attached to the first electrode by a phosphorothioate or a phosphonate.

203. (Previously presented) The molecular sensing apparatus of claim 197

wherein the biological macromolecule is attached to said first electrode by a linker.

204. (Previously presented) The molecular sensing apparatus of claim 203

wherein said linker is selected from the group consisting of DFDNB, DST, ABH, ANB-NOS, EDC, NHS-ASA, and SIA.

205. (Currently amended) The molecular sensing apparatus of claim 1 wherein a

first biological macromolecule is attached to ~~the~~ said first electrode and a second biological macromolecule is attached to ~~the~~ said second electrode.

206. (Previously presented) The molecular sensing apparatus of claim 1 wherein said first electrode comprises a surface with a shape selected from the group consisting of convex, concave, textured, corrugated, patterned uniformly, and randomly patterned.

207. (Previously presented) The molecular sensing apparatus of claim 199 wherein said nucleic acid is deoxyribonucleic acid or ribonucleic acid.

208. (New) The molecular sensing apparatus of claim 1, wherein said first electrode and said second electrode are separated by less than 20 nanometers.

209. (New) The molecular sensing apparatus of claim 208, wherein said first electrode and said second electrode are separated by less than 15 nanometers.

210. (New) The molecular sensing apparatus of claim 209, wherein said first electrode and said second electrode are separated by less than 10 nanometers.

211. (New) The molecular sensing apparatus of claim 166, wherein said first electrode and said second electrode are separated by less than 20 nanometers.

212. (New) The molecular sensing apparatus of claim 211, wherein said first electrode and said second electrode are separated by less than 15 nanometers.

213. (New) The molecular sensing apparatus of claim 212, wherein said first electrode and said second electrode are separated by less than 10 nanometers.